

### REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

In the specification, the Title has been amended to better reflect the subject matter of the application. In addition, the specification has been amended on page 1, line 1 to include a cross-reference to related applications.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claims 1, 2, 10, 12, 14, 16-26, and 29-50 are requested to be cancelled without prejudice.

Claims 3-5, 7, 9, and 11 are currently being amended in order to advance prosecution of this application.

Claim 51 is currently being added. Claim 51 depends from claim 3, which is currently under consideration as part of elected Group 2, drawn to DNA of SEQ ID NO:4, as defined by the Examiner. As such, Applicants request that the Examiner consider the merits of claim 51.

Applicants respectfully contend that support for amended claims 3-5, 7, 9, 11 and new claim 51 is provided in the specification and claims as filed.

After amending the claims as set forth above, claims 3-9, 11, 13, 15, 27-28, and 51 are now pending in this application. Claims 13, 15, and 27-28 have been withdrawn from consideration as a result of the restriction requirement. Claims 3-9, 11 and 51 are currently under consideration.

**Claims Cancelled and Withdrawn**

Applicants have cancelled claims 1, 2, 10, 12, 14, 16-26, and 29-50 without prejudice. Applicants reserve the right to file one or more divisional applications related to the subject matter of the cancelled claims. As previously noted, Applicants requested in Form PTO-1390, submitted February 20, 2002, that claims 12, 14, 18, 20, 21, 23, 24, 25, 26, and 30-50 be cancelled. Applicants have enclosed a copy of Form PTO-1390 herewith.

Claims 13, 15, and 27-28 have been withdrawn from consideration but depend from or have been amended to depend from base claims that relate to products which are currently under consideration. Claims 13, 15, and 27-28 relate to methods for using the products which are currently under consideration. As such, Applicants request that the Examiner rejoin the withdrawn claims if the Examiner determines that the base claims are allowable.

**Specification/Continuation Data**

In the Office Action dated September 30, 2004, the Examiner objected to the specification for failing to include a cross-reference to related applications. Applicants have amended the specification at page 1, line 1 to include a cross-reference to related applications and request that the Examiner reconsider and withdraw the objection.

**Claim Objections**

In the Office Action, the Examiner objected to claims 3-9 for being in improper dependent form. Applicants have amended claims 3-9 to present the claims in proper independent/dependent form and request that the Examiner reconsider and withdraw the objection.

### **Written Description**

In the Office Action, the Examiner rejected claims 3, 6-9, and 11 under 35 U.S.C. § 112, first paragraph, “as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.” Applicants respectfully traverse the rejection.

First, Applicants note that the Examiner contends that the “claims are directed to a genus of polynucleotide molecules [that encode polypeptides] *with no defined function[s] associated with [them]*.” Applicants respectfully disagree. The specification relates to Human Lyases in general and describes *carbonic anhydrases* in particular. At paragraph [0130], the specification states:

SEQ ID NO:1 is 59% identical, from residue M1 to residue A239, to human carbonic anhydrase I (GenBank ID g179793) as determined by the Basic Local Alignment Search Tool (BLAST). (See Table 2.) The BLAST probability score is 6.9e-80, which indicates the probability of obtaining the observed polypeptide sequence alignment by chance. SEQ ID NO:1 also contains a eukaryotic-type carbonic anhydrase domain as determined by searching for statistically significant matches in the hidden Markov model (HMM)-based PFAM database of conserved protein family domains. (See Table 3.) Data from BLIMPS, MOTIFS, and PROFILESCAN analyses provide further corroborative evidence that ***SEQ ID NO:1 is a carbonic anhydrase***. In an alternative example, SEQ ID NO:2 is 59% identical, from residue M1 to residue 1459, to *Xenopus laevis* ornithine decarboxylase-2 (GenBank ID g6746571) as determined by the Basic Local Alignment Search Tool (BLAST). (See Table 2.) The BLAST probability score is 1.9e-148, which indicates the probability of obtaining the observed polypeptide sequence alignment by chance. SEQ ID NO:2 also contains an ornithine decarboxylase domain as determined by searching for statistically significant matches in the hidden Markov model (HMM)-based PFAM database of conserved protein family domains. (See Table 3.) Data from BLIMPS and MOTIFS analyses provide further corroborative evidence that ***SEQ ID NO:2 is a carbonic anhydrase***. In yet another example, SEQ ID NO:3 is 58% identical, from residue

E30 to residue R314, to human adenylate kinase (GenBank ID g3283386) as determined by the Basic Local Alignment Search Tool (BLAST). (See Table 2.) The BLAST probability score is  $5.7e-94$ , which indicates the probability of obtaining the observed polypeptide sequence alignment by chance. SEQ ID NO:3 also contains a eukaryotic-type carbonic anhydrase domain as determined by searching for statistically significant matches in the hidden Markov model (HMM)-based PFAM database of conserved protein family domains. (See Table 3.) Data from BLAST-DOMO, BLAST-PRODOM, BLIMPS, and PROFILESCAN analyses provide further corroborative evidence that ***SEQ ID NO:3 is a eukaryotic-type carbonic anhydrase.***

As such, Applicants clearly indicated that the claimed sequence and other sequences disclosed in the specification are carbonic anhydrases. Applicants have amended the Title of the application accordingly. As discussed further below, Lehtonen *et al.* subsequently have confirmed that SEQ ID NO:4 encodes at least a portion of a human carbonic anhydrase. (See Lehtonen *et al.*, J BIOL. CHEM. 2004 Jan 23;279(4):2719-27, [hereinafter "Lehtonen *et al.*"], copy enclosed herewith as part of an Information Disclosure Statement and listed on Form PTO/SB/08).

In addition, Applicants have amended claim 3 to recite "a biologically active fragment of SEQ ID NO:1, ***wherein the fragment has carbonic anhydrase activity***" and an "immunogenic fragment comprising at least about 10 amino acids of SEQ ID NO:1, ***wherein the fragment has immunological activity of carbonic anhydrase.***" Claim 11 has been amended to recite "a naturally occurring polynucleotide comprising a polynucleotide sequence at least 90% identical to a polynucleotide sequence ***of at least about 60 contiguous nucleotides of SEQ ID NO:4.***" Therefore, Applicants respectfully contend that one skilled in the art would reasonably conclude that Applicants were in possession of the claimed invention at the time the application was filed and request that the Examiner reconsider and withdraw the rejection.

### **Enablement Rejection**

In the Office Action, the Examiner rejected claims 3, 6-9, and 11 under 35 U.S.C. § 112, first paragraph, stating that “because the specification, while being enabling for an isolated nucleic acid (or polynucleotide) sequence of SEQ ID NO:4 encoding a specific lyase (?) of SEQ ID NO:1, does not reasonably provide enablement for any fragment, [biologically active or immunogenic] of SEQ ID NO:1 or 4; or that encoding a protein having 90% homology to SEQ ID NO:1 or a nucleic acid having 90% similarity to SEQ ID NO:4.” Applicants respectfully traverse the rejection.

As noted above, claim 3 has been amended to recite “a biologically active fragment of SEQ ID NO:1, *wherein the fragment has carbonic anhydrase activity*” and “an immunogenic fragment comprising at least about 10 amino acids of SEQ ID NO:1, *wherein the fragment has immunological activity of carbonic anhydrase.*” Claim 11 has been amended to recite “a naturally occurring polynucleotide comprising a polynucleotide sequence at least 90% identical to a polynucleotide sequence of *at least about 60 contiguous nucleotides of SEQ ID NO:4.*”

In regard to the limitation “a biologically active fragment of SEQ ID NO:1, wherein the fragment has carbonic anhydrase activity,” as recited in claim 3, the specification describes an exemplary assay for carbonic anhydrase activity. In addition, assays for measuring carbonic anhydrase activity are well known in the art. Because carbonic anhydrases have been studied and are well known in the art, one skilled in the art would know how to identify “specific catalytic amino acids” and/or “structural motifs essential for activity/function which must be preserved” without “undue experimentation.”

In regard to the limitation “an immunogenic fragment comprising at least about 10 amino acids of SEQ ID NO:1, wherein the fragment has immunological activity of carbonic anhydrase,” as recited in claim 3, the specification describes methods for generating antibodies to fragments of the disclosed polypeptides that encode carbonic anhydrases. Further, one skilled in the art would know how to identify immunogenic fragments of the polypeptide.

In regard to the limitation “a naturally occurring polynucleotide comprising a polynucleotide sequence at least 90% identical to a polynucleotide sequence of at least about 60 contiguous nucleotides of SEQ ID NO:4,” as recited in claim 11, Applicants contend that one skilled in the art would know how to make and/or isolate the recited polynucleotide sequence without “undue experimentation.” Therefore, Applicants contend that the claims are fully enabled and request that the Examiner reconsider and withdraw the rejection.

**35 U.S.C. § 101, statutory subject matter**

In the Office Action, the Examiner rejected claims 7 and 8 under 35 U.S.C. § 101 for being “directed toward non-statutory subject matter.” The Examiner noted that “[t]his rejection may be overcome by amending the claims to recite the wording such as ‘An isolated cell transformed with the....’” Applicants have adopted the Examiner’s recommendation and have amended the claims accordingly. Applicants request that the Examiner reconsider and withdraw the rejection.

**35 U.S.C. § 101, utility**

In the Office Action, the Examiner rejected claims 3-9 and 11 under 35 U.S.C. § 101, stating that “the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.” Applicants respectfully traverse the rejection. As disclosed in the specification and as confirmed by Lehtonen *et al.*, the claimed sequences specifically relate to carbonic anhydrases (“CAs”). Further, a number of disease states are related to variations in CA activity.

The disclosed polypeptide sequence of SEQ ID NO:1 is 100% identical to amino acids 1-242 of the polypeptide disclosed by Lehtonen *et al.* and termed “carbonic anhydrase XIII” or “CA XIII”. (See Lehtonen *et al.*, at page 2722.) As described by Lehtonen *et al.*, CA XIII includes 262 amino acids.

Lehtonen *et al.* provide a structural model for CA XIII. (*See id.*, at pages 2721 and 2724.) Further, Lehtonen *et al.* show that the structural model revealed a globular molecule with high structural similarity to other carbonic anhydrases. (*See id.*) Lehtonen *et al.* also show that recombinant mouse CA XIII has catalytic activity similar to other carbonic anhydrases. (*See id.*)

Lehtonen *et al.* show that CA XIII is expressed in a number of tissues including thymus, small intestine, spleen, prostate, ovary, colon, and testis. In mouse, positive tissues included the spleen, lung, kidney, heart, brain, skeletal muscle, and testis. (*See id.* at pages 2721, and 2723-2726.) Lehtonen *et al.* conclude that “the predicted amino acid sequence, structural model, distribution, and activity data suggest that CA XIII represents a novel enzyme, ***which may play important physiological roles in several organs.***” (*See id.* at page 2719.) Lehtonen *et al.* indicate that tests are underway to determine whether “CA XIII inhibition may constitute a new pharmacological target.” (*See id.* at page 2727.)

In particular, Lehtonen *et al.* state that “[o]ne could hypothesize that CA XIII might contribute to normal fertilization process by producing the appropriate bicarbonate concentration in the cervical and endometrial mucus,” and that “it would be interesting...to determine the role of this novel enzyme on spermatogenesis and fertilization capacity.” (*See id.*) Similarly, the specification of the instant application indicates that “CAs participate in a variety of physiological processes that involve pH regulation, CO<sub>2</sub> and HCO<sub>3</sub> transport, ion transport, and water and electrolyte balance. (*See* paragraph [0006].) Further, the specification indicates that “[a] positive correlation has been observed between CA I and CA II reactivity and endometriosis. (*See* paragraph [0009], citing Brinton *et al.*, (1996) ANN. CLIN. LAB. SCI. 26:409-420; and D’Cruz *et al.*, (1996) FERTIL. STERIL. 66:547-556). Endometriosis is known to cause infertility.

As such, Applicants contend that the specification provides a specific, substantial, and credible utility for the claimed sequences as confirmed by Lehtonen *et al.* Applicants request that the Examiner reconsider and withdraw the rejection.

**35 U.S.C. § 112, second paragraph**

In the Office Action, the Examiner rejected claims 3-9 under 35 U.S.C. § 112, second paragraph, “as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” In particular, the Examiner contended that the term “biologically active fragment” renders the claims indefinite “because it is unclear what activity is associated with such a biological function.” Applicants have amended claim 3 to recite “a biologically active fragment of SEQ ID NO:1, *wherein the fragment has carbonic anhydrase activity.*” As such, Applicants request that the Examiner reconsider and withdraw the rejection.

**35 U.S.C. § 102**

In the Office Action, the Examiner rejected claims 1 and 11 under 35 U.S.C. § 102 as being anticipated by Lowe *et al.* The Examiner stated that “[Lowe *et al.*] inherently teaches 15 or more identical nucleotides encoding...5 or more identical amino acid fragments.” As such, the Examiner contended that Lowe *et al.* “reads upon Applicants’ biologically active fragment (see claim 1).”

Applicants have cancelled claim 1. As amended, claim 3 recites “a biologically active fragment of SEQ ID NO:1, *wherein the fragment has carbonic anhydrase activity*” and an “immunogenic fragment *comprising at least about 10 amino acids of SEQ ID NO:1, wherein the fragment has immunological activity of carbonic anhydrase.*” Applicants contend that Lowe *et al.* does not anticipate claim 3 as amended.

Claim 11 has been amended to recite “a naturally occurring polynucleotide comprising a polynucleotide sequence at least 90% identical to a polynucleotide sequence *of at least about 60 contiguous nucleotides of SEQ ID NO:4.*” Applicants contend that Lowe *et al.* does not anticipate claim 11 amended. As such, Applicants request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 102.

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.



The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant(s) hereby petition(s) for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date 12/30/2004

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